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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,549	01/11/2002	Willy Deleersnijder	01975.0032	8772

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EXAMINER	
GUCKER, STEPHEN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,549	DELEERSNIJDER ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *10,13-22 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11,12,23 and 25-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

3. Claims 1-9, 11-12, 23 (in part), 25, and 26-33 (in part - limited to polynucleotides by original election) are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a well-established utility or a disclosed specific and substantial credible utility for reasons of record and the following. The instant claims are drawn to multiple genuses of isolated nucleic acids that share 80% or 90% sequence identity to SEQ ID NO:1 or a nucleotide sequence encoding SEQ ID NO:2 (a receptor protein called IGS1), the complementary sequences thereof, or various expression systems (i.e. vectors), host cells, or methods of expressing the proteins encoded by the multiple genuses of isolated nucleic acids. The underlying asserted utility for the encoding nucleic acid sequences for IGS1 is that it is a member of the G-protein coupled receptor (GPCR) superfamily, and therefore has utility for disease diagnosis, therapy, drug screening, genetic analysis for mutations for inherited disorders, and as a chromosomal marker.

First, there is no well-established utility for the instant nucleic acids or the encoded receptor protein. Applicants have not taught what the instant receptor protein is a receptor for, therefore, no known ligand exists that binds to and activates the encoded instant protein. Likewise, no known ligand exists that binds to and inhibits the

activation of the encoded instant protein. Therefore, it is completely unknown what biological processes the instant protein or its underlying encoding nucleic acids are associated with or involved in. It is not known if the receptor when activated by its endogenous ligand produces a stimulatory or inhibitory signal to the cell that the receptor is a part of. In fact, the nature of the signal that the instant receptor transduces when its unknown ligand binds to it is also unknown. Because the endogenous or exogenous (i.e. drug) ligand that would bind to the instant receptor has not yet been discovered, the instant receptor is called an "orphan receptor" by those of ordinary skill in the art. The instant receptor and its encoding nucleic acids have no well-established utility because no known compound exists which binds to the receptor and produces or inhibits its biological function, the specific biological processes in which the receptor participates in are unknown, and the second messenger or any other known signal transduction means by which this receptor could operate has not been demonstrated in any specific or substantial way by the teachings of the instant disclosure.

As stated therein, the instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v.*

Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to nucleic acids of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the nucleotides of the instant application can be used for diagnosis, prevention and treatment of diseases or disorders as stated at pages 3-4 of the specification. Until some actual and specific significance can be attributed to the protein identified in the specification as IGS1, or the gene encoding it, the instant invention is incomplete. The DNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to G-protein coupled receptors (GPCR). Because the various members of the GPCR protein superfamily have different sites of action and different biological effects, it is not clear if

the protein of the instant application would be a receptor for a growth factor, an inhibitor of cell proliferation, a binding protein, a hormone, a cytokine, a lymphokine, a neurotransmitter, or even possibly a transcription factor. In the absence of a knowledge of the ligand to which IGS1 binds, or the biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a specific and substantial "real world" use for IGS1, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

Any unique nucleic acid sequence can serve as a chromosomal marker. Therefore, the instant invention does not have a specific utility as a chromosomal marker that is not shared with any and every other nucleic acid sequence that encodes a GPCR.

4. Claims 1-9, 11-12, 23 (in part), 25, and 26-33 (in part - limited to polynucleotides) also are rejected under 35 U.S.C. 112, first paragraph for reasons of record and the following. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments and affidavit filed 2/19/04 are not persuasive to overcome either the utility or enablement rejections of record because the affidavit adds additional teachings in relation to an animal model of Parkinson's disease that go far beyond what was originally filed in the specification. On pages 3-4 of the instant specification,

Parkinson's disease is included as one of approximately ninety separate diseases, disorders, or dysfunctions that the instant invention allegedly can be used for, or has a role in, the diagnosis, prevention, or amelioration of the aforementioned maladies, collectively referred to by the Applicant as "the Diseases" (page 3, line 23). The specification also states that the instant invention is not limited to the ninety or so "Diseases" recited, but may have a role in any psychiatric or CNS disorder, kidney disease, cardiovascular disease, gastrointestinal disease, gynecological disorders, inflammations, infections of any kind, cancer, immune disorders, pain, chemotherapy induced injuries, etc. However, the specification provides no specific or substantial teachings as to the utility of the instant nucleic acid in relation to any specific disorder or group of disorders, and no 'real world' question posed by a skilled artisan (i.e. a physician) could be answered by the specification without undue further research and experimentation. For example, given the instant disclosure and any one of the specific diseases recited, such as Parkinson's disease, what course of action would a physician take if the nucleic acid of the instant invention was found to decrease in Parkinson's disease? The knee-jerk reaction might be to say that if a level of the nucleic acid encoding a receptor goes down in a disease, one would want to somehow increase the level of the receptor or give an agonist drug to stimulate the remaining receptors. Unfortunately, without more research or knowledge of the utility and function of the receptor, one cannot assume the knee-jerk reaction is correct because suppose the decrease in the nucleic acid level is not the harmful result of some pathological process, but a beneficial result of the brain's attempt to compensate for the underlying disease.

For example, if you are in a car accident and suffer a facial injury that results in damage to the skin and nerves of your face, the body tries to repair itself by increased production of growth factors to stimulate regrowth and repair of the damaged tissues. In which case, your physician would want to encourage the production of factors to help neuronal regeneration, but may want to discourage the production of factors that would increase scar formation. The physician would need to know which specific growth factors should be increased to encourage nerve regeneration, and which factors would have to be inhibited by antagonist drugs or otherwise reduced in order to minimize scar formation. The same situation exists in the brain where the skilled artisan would have to know the utility of what an increase or decrease of the instant nucleic acid meant in terms of the specific disease process of Parkinson's disease. Such disclosure is conspicuously absent in the instant specification. Support for the Examiner's contention can even be found in Applicant's affidavit filed 2/19/04. Even though Applicant has reported in the affidavit that the instant nucleic acid decreases in an animal model of Parkinson's disease (see affidavit page 4, point number 25), this post-filing disclosure is immediately followed by the statement that "It is also likely that agonists and antagonists of IGS1 should have a significant role in treating and preventing Parkinson's disease" (see affidavit page 4, point number 26, underlining mine). Even though Applicant now knows that the nucleic acid level of the instant invention is decreased in certain brain regions in an animal model of Parkinson's disease, such disclosure still makes it impossible for the Applicant to make a simple affirmative statement that either drugs that turn on the receptor (agonists) or drugs that do exactly the opposite (block or turn

off the receptor (antagonists)) should be used to treat the disease! Why? It is the Examiner's contention that Applicant cannot make such a statement because the utility of the instant invention was still unknown even at the time of the filing of the affidavit, 43 months after the filing of the international application on which this U.S. application is based.

In terms of diagnosis of Parkinson's disease, the Examiner notes that the specification teaches that the nucleic acid of the instant invention is present in multiple brain areas, including the putamen and caudate nucleus, among other regions (see Figure 3). The specification is again conspicuously silent as to whether an increase or decrease in the level of the instant nucleic acid is indicative of any one of the ninety or so boiler-plate disorders recited as "the Diseases." The affidavit filed 2/19/04 introduces new matter into the instant application by indicating that in an animal model of Parkinson's disease, the nucleic acid of the instant invention decreases in the nucleus accumbens, dorsomedial caudate putamen, and the ventromedial caudate putamen, but does not change in the dorsolateral caudate putamen or the ventrolateral caudate putamen (page 3). These results were not present in the specification as filed, and there is no guidance in the disclosure to subdissect any areas of the human body or the brain, let alone the putamen and caudate nucleus specifically, to look for these changes as compared to any other brain region shown in Figure 3, or to selectively look for these specific changes in Parkinson's disease as compared to the other ninety or so diseases listed. To reiterate once again,

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the

> public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Finally, Applicant argues that the instant invention has utility and is enabled because it is present in the limbic system of the brain. Similar to the Examiner's arguments regarding Parkinson's disease, the presence or absence of a nucleic acid encoding an orphan receptor for which no known ligand exists and which has a completely unknown function, such a nucleic acid simply does not possess a specific or substantial utility until further research is performed that provides guidance as to what the biological significance of the instant invention is in terms of diagnosis or treatment of a limbic system disorder.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961. The fax phone number for this Group is currently (703) 872-9306.

SG

Stephen Gucker

July 21, 2004

Brenda Brumback

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